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The workshop entitled "High-Field Effects and Fast Pulse Responses in Bio-Systems" was successfully held at the Hyatt Regency Hotel, Albuquerque, NM on Sunday, 19 October 2003. There were 26 participants with presentations chosen to highlight work on fast pulse effects in biological cells and tissues. A 132-page volume of workshop proceedings was later produced and distributed to participants.

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Report on the DEIS Bio-Workshop
"High-Field Effects and Fast Pulse Responses in Bio-Systems"
held at the Hyatt Regency Hotel, Albuquerque, New Mexico on
Sunday, 19th October (in association with the IEEE CEIDP 2003).

W. Mike Arnold
Chair – 2003 Workshop
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Introduction

The organization of this event was "sparked" by the success of the Workshop on "Dielectric Properties and Electrical Breakdown of Biological Membranes", organized by Karl Schoenbach and which had taken place at the 2002 CEIDP.

As indicated by the title of the 2003 Workshop, the presentations were chosen to highlight work on fast pulses in biological cells and tissues.

Due to the availability of a number of manuscripts from contributors, it was possible to produce a 132-page volume of Workshop Proceedings.

There were 26 full attendees at the Workshop. It is believed that all of these also attended the CEIDP. One other CEIDP attendee purchased a copy of the Workshop Proceedings.

The Presentations

The first session covered some general aspects of electro-pulse effects, starting with "Biotechnological Applications of High-Voltage Pulsed Electric Field". In this talk Prof. Sato of Gunma University, Japan introduced his extensive work on pulsed field applications (electro-release, electro-sterilization, etc.). This was actually a two-part lecture, and in the second part Dr. Ohshima from the same institute presented his results on electric-field-induced degradation of bio-polymers, particularly DNA and RNA.

In the second presentation, Prof. R.C. Lee of the University of Chicago talked on "Electrical Injury: Biophysical Mechanisms and New Therapeutic Agents". This presentation covered some of the speaker's considerable work on the damage that can be done to biological systems, and cell membranes in particular, by electrical currents. A significant part of the material concerned the ability of amphiphilic block copolymers such as poloxamers and poloxamines to ameliorate the effects of electric shock. The most common cause of such shock may be exposure to DC or power line frequencies, yet it is the chair's opinion that similar materials may be used to modulate the membrane disturbances produced by micro- and nano-second pulses.

After the morning break for tea or coffee, K.V.I.S. Kaler of the University of Calgary (Canada) presented a talk on "Cellular and Particle DEP in Microfluidic Channels". As demonstrated by Prof Kaler, the combination of electrical handling of bioparticles with microfluidics is becoming very useful. Devices can be fabricated easily and quickly by the use of silicone elastomer (PDMS). It seems likely that similar techniques of fabrication and cell handling will be used in conjunction with fast pulse work where this is to be done on the small scale.

The final presentation of the morning was "Ultrashort Electrical Pulses Open a New Gateway into Biological Cells", by K. Schoenbach (Old Dominion University). There were several

significant aspects of this talk, the first being that it narrated the history of the discoveries leading to the use of sub-microsecond pulses on organisms. Beyond that it covered some of the interesting bio-effects such as the induction of apoptosis in some but not all cell populations, as well the detection of related signals such as calcium bursts and release of mitochondrial cytochrome c. Some indication of the specialised high-voltage engineering involved, such as transmission-line generators of the Blumlein configuration, was also given.

After a 1-hour break for lunch, the experimental fast-pulse theme was continued with the talk "Non-Invasive Electroperturbation of Membrane Phospholipid Asymmetry and Intracellular Calcium Distribution With Nanosecond Pulses" by T. Vernier of the University of Southern California and MOSIS (the USC fabrication facility). The techniques reported were largely complementary to that from the Old Dominion University: MOSFET generators are used instead of spark-gap, and a different selection of cell types are exposed. Use of novel fluorescent membrane probes was also reported. In spite of differences in technique, the results showing that nano-second pulses can cause significant changes within the cell without electroporation of the plasmalemma, and that calcium bursts, plasmamembrane PS externalisation, and caspase activation can all occur after exposure, were essentially in agreement.

One way of investigating the mechanism of action of fast pulses is to model their effects. In the first presentation to address this area, J. C. Weaver of MIT presented his group's work in "A Model for the Induction of Cell Apoptosis by Submicrosecond, Megavolt-per-meter Electric Field Pulses". The approach, that of using the Transport Lattice Solution based on the circuit emulator SPICE 3f5, is able to yield numerical solutions to 2-D and 3-D models of cells and tissues. The response to the MV/m pulses was characterized as a "super-electroporation" in that all membrane, external and internal, must be affected even if only transiently.

A further talk on the subject: "Modeling Studies of Cell Response to Ultrashort, High-Intensity Electric Fields: Implications for Intracellular Electro-Manipulation" was given by R. Joshi of the Old Dominion University. The approach here was in some ways similar to that of J.C. Weaver's, but also included more mechanistic hints such as the gating of proton channels. It was used to predict differences in the susceptibilities to ns-pulses of different cell types, especially cancerous as opposed to normal, based on literature values for the permittivity and conductivity of their membranes and aqueous regions.

The solid-state pulse equipment, the fast and sensitive optics, and the pulse exposure chamber microfabrication used in much of the recent work from USC was described in more detail in "Non-Invasive Approaches to Nano-Biology Through Advanced Pulsed Power" by Y. Sun of the University of Southern California. Not only the present generation of pulsers, but also equipment as yet under construction, was described.

Discussion Session

The workshop finished with a "Roundtable Discussion". Several comments were made and some new topics were covered:

The noteworthy lack of externalization of PS in some cells (e.g. glioma cells).

The inability of many cancer cells (except Jurkat cells) to undergo apoptosis.

The specification of preferred cell lines? Apparently HL60 and Jurkat are good candidates as "standards" for further work.

Possibilities may exist for using the technology for "gene therapy".

There appears to be a need to convince the "apoptosis community" to look at ns-pulsing as a useful technique.

The methods and observations could be useful for trauma-readiness, e.g. for treating astronauts exposed to solar flares.

It was decided to try to continue the forum by way of a special issue of a suitable journal such as the DEIS Transactions or the Electrical Insulation Magazine.

Acknowledgment

It remains for this author to thank the contributors for their generosity both with their time and, in many cases, with printed material for the Workshop volume.

The workshop would not have been possible without the material support of the following organizations: the Air Force Office of Scientific Research, the Office of Naval Research, and the IEEE Dielectrics and Electrical Insulation Society. Sincere thanks are due to these organizations, as well as to Arizona State University for administering the funds without charges.

Most especial thanks are due to Vice Chair, Raji Sundararajan of ASU East, who co-ordinated many aspects as well as acting as Workshop Treasurer.